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This study is designed to assess the effectiveness of positron emission tomography (PET) with fluorodeoxyglucose in patients with metastatic breast cancer undergoing high dose chemotherapy with stem cell rescue. It includes patients enrolled on two high dose chemotherapy trials (PBT-1 and UCPP # 3195). So far, 31 patients have been enrolled in the protocol, and the study is procceding as planned. We have performed a preliminary analysis of the PET studies of 24 patients performed before high dose chemotherapy. In this subgroup of patients, 17 had active disease demonstrated on the PET study, and 7 had no evidence of metabolically active disease. Two subjects had disease involvement demonstrated only on PET imaging and proven at pathology or follow-up. Several repeat studies have been performed and will be analyzed when enough prognostic information becomes available. Patient accrual is ongoing and the study is proceeding as scheduled. PET FDG imaging is a promising tool that can potentially predict early therapeutic failure.

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INTRODUCTION

Positron emission tomography (PET) was introduced as a research modality to investigate physiological and biochemical alterations in the brain and heart[1]. Many radiopharmaceuticals have been introduced for the study of various organs, but ^{18}F-fluoro-2-deoxy-2-glucose (FDG) is generally considered the most useful radiopharmaceutical for the diagnosis of various tumors. Breast cancers have enhanced glycolytic activity and have a significant overexpression of glucose transporters[2]. Tumor hypoxia has been shown to increase FDG retention[3], and the tracer has been shown to be mainly incorporated in malignant cells[4].

There are now several reports of studies of patients with breast cancer, suggesting that the PET-FDG technique is effective in diagnosing and following patients with primary and metastatic breast tumors[5-10]. A recent retrospective study on the efficacy of PET in detecting axillary lymph node involvement has suggested potential cost savings by reducing the number of axillary dissections for breast cancer. Almost 74,000 women (75% patients) with primary breast tumors could potentially be spared axillary dissection based on the sensitivity and specificity of PET-FDG imaging to detect lymph node involvement[11].

Some groups have reported on the use of PET to evaluate tumor response to therapy. Wahl[12] described the use of PET-FDG for monitoring the treatment response of primary breast cancer. Eleven patients with large primary cancers were studied before chemohormonotherapy and at four times after initiating treatment (at days 8, 21, 42 and 63). The quantitative PET scans showed a rapid decrease in tumor glucose metabolism in all eight patients whose cancers responded clinically, but no change in the 3 non responding patients. Qualitative (visual) analysis gave the same result. The metabolic change preceded clinical evidence of response (mammographic change), and in some patients the mammogram was difficult to interpret due to dense breast tissue. Thus, the PET-FDG appeared to be an early and accurate predictor of breast cancer response. Huovinen et al[13], using

^{11}C-Methionine, reported changes in uptake in soft tissue lesions of eight patients treated with chemotherapy, hormone therapy or radiation. The PET responses correlated with clinical responses; uptake increased in those who showed progressive disease, and decreased in patients with stable or improving lesions. Jansson et al[14] studied sixteen patients with locally advanced and metastatic breast cancers receiving chemotherapy. They noted a decrease in uptake (^{11}C-Methionine or FDG) compared to pretreatment scans in eight of twelve responders after the first course of therapy (scans were performed at 6 - 13 days after treatment). Scans done after a third chemotherapy course showed a decrease in all clinical responders. These responses were noted in breast, axillary nodes, pleura and liver.

The purpose of our study is to evaluate the effectiveness of PET-FDG in patients with metastatic breast cancer who are also being treated with high dose chemotherapy and stem cell rescue. The hypotheses of the study are as follow:

1) Active tumor sites shown by anatomical imaging methods will be associated with high levels of metabolic activity while inactive sites will be reflected by low levels of FDG uptake.
2) Reduction in tumor metabolic activity of tumors will be an early predictor of response to high dose chemotherapy.
3) Patients with no abnormal FDG uptake prior to high dose chemotherapy will live longer than patients with tumor that are metabolically active.

The use of PET in this setting is potentially cost-saving considering the high costs of stem cell rescue. Non responders do not need to undergo further chemotherapy with consequent suffering and high costs, when palliation is more appropriate. On the other hand, the ability to predict the response to chemotherapy in responders might enable the physician to modulate the treatment for each patient.

The study includes a homogeneous group of patients entered on two University of Pennsylvania studies for the treatment of breast cancer with high dose chemotherapy. The chemotherapy protocols are protocol UPCC #3195 and Protocol PBT-1.

BODY

Materials and Methods

Patient Selection:

Patients selected for entry in this study women accepted for one of the two high dose chemotherapy protocols utilizing autologous stem cell support at the University of Pennsylvania. The two protocols are: Protocol UPCC #3195 ("Phase II Pilot Study of High Dose Chemotherapy With Melphalan Followed by Cyclophosphamide, Thiotepa, and Carboplatin with Cyclophosphamide and G-CSF Augmented Peripheral Stem Cell Support For Women With Responding Metastatic Breast Cancer") or Protocol PBT-1 ("Phase III Randomized Comparison of Maintenance Chemotherapy with Cyclophosphamide, Methotrexate and 5-FU vs. High Dose Chemotherapy with Cyclophosphamide, Thiotepa and Carboplatin and autologous bone marrow support for women with metastatic breast cancer who are responding to conventional induction chemotherapy").

Chemotherapy Studies:

UPCC #3195: This study is a University of Pennsylvania Cancer Center single institutional trial designed for patients with metastatic disease or inflammatory breast cancer. Those patients with no evaluable disease or a documented complete or partial response to standard chemotherapy are treated with high dose sequential chemotherapy and peripheral stem cell rescue. Patients receive high dose Cyclophosphamide followed by G-CSF to stimulate stem cell production. This is followed by apheresis to harvest stem cells. When blood count recovery has occurred, high dose

Melphalan is administered to the patient followed by infusion of one-third of the collected stem cells. Twenty-one days later, the patient is treated with high dose chemotherapy regimen consisting of Cyclophosphamide (1500 mg/m^2), Thiotepa (125 mg/m^2) and Carboplatin (200 mg/m^2), each drug being given daily for four days. This is followed by peripheral stem cell reinfusion.

PBT-1: The purpose of this study is to compare the time to treatment failure, overall survival and toxicity in patients with metastatic breast cancer who are treated with conventional chemotherapy alone or conventional dose chemotherapy followed by high dose chemotherapy and autologous bone marrow rescue. Patients are entered in this trial prior to receiving any chemotherapy for metastatic disease. They will then receive Cytoxan, Adriamycin and 5-FU. At the end of 4 - 6 cycles of treatment for metastatic disease, the patients will be reevaluated. Those in a partial response or in a complete response will then be randomized either to continue the same chemotherapy (or change from Adriamycin to Methotrexate after a total dose of Adriamycin has been given) until relapse or to receive high dose therapy and autologous bone marrow treatment with no further therapy after the transplant. The high dose regimen consists of 4 days of Cyclophosphamide (1500 mg/m^2), Thiotepa (125 mg/m^2) and Carboplatin (200 mg/m^2). The patients who undergo bone marrow transplantation are selected for this PET study.

PET Camera:

The PENN PET 240H camera, manufactured by UGM, has been used extensively over the last 5 years for FDG and ^{15}O-water brain studies, FDG whole-body cancer studies, and FDG/^{13}N-ammonia cardiac studies. This scanner is based on NaI(Tl) position-sensitive detectors, which leads to high spatial resolution, 5.5 mm (FWHM) in the transverse and axial directions, and fine spatial sampling, 2 mm in both the transverse and axial directions[15]. The fine axial sampling, in particular, is a unique advantage of the system, leading to a maximum of 64 slices, which helps us achieve accurate quantification and reduce the partial volume effect in PET[16]. To achieve the maximum sensitivity, the scanner operates as a full-time 3D system, without septa.

Whole body scanning technique:

The whole-body scanning is carried out according to the ongoing protocol in our laboratory. Currently, 114 μCi/kg is injected intravenously in the patient. Forty minutes later, the patient is positioned supine in the scanner, feet first, with her arms extended and folded behind the neck. The scanner is then moved by successive 6 cm steps to image the desired areas. This position allows imaging the entire supraclavicular and axillary lymph node sites. A post-emission transmission scan is then obtained. The scanning area includes the entire chest and supraclavicular regions.

Image Reconstruction techniques:

All the tomographic images are reconstructed with filtered back projection with a Hanning filter for a final image resolution of approximately 6 mm. We also reconstructed all studies with a new iterative reconstruction algorithm, the ordered subset expectation maximization algorithm[17, 18], to further improve image quality for qualitative and quantitative interpretation.

Qualitative interpretation:

The images are read by two experienced observer on the whole body images, without attenuation or scatter correction. The readers are blinded to clinical and other radiological information. Regions of the body were considered abnormal according to the following criteria: nodal disease was identified when a clearly defined nodular abnormality could be demonstrated in lymph node groups, exceeding regional average activity; local bone involvement was considered for areas with focally increased tracer uptake higher than maximal marrow activity; diffuse bone marrow involvement was considered if the tracer retention exceeded that of liver activity; liver and other soft tissue lesions were considered positive if clear nodular areas of increased tracer retention were identified, exceeding regional average activity. Increased areas of tracer retention corresponding to sites of normal physiologic distribution (urinary tract, bowels, muscle groups, heart, thyroid, etc.)

were not considered abnormal. The rating scale utilized for recording the abnormalities is indicated in table 1.

Quantification

Quantitative analysis will be carried out on attenuation and scatter corrected images by assigning regions of interest (ROI) over the area(s) of abnormal uptake visually determined. One quantitative measure of the uptake of a given isotope in a tumor is the standardized uptake value (SUV)[19] which is defined as:

SUV = (uptake activity/gram of tissue)/(injected activity/gram of patient weight).

In malignant tumors, SUV > 2, sometimes reaching as high as 9-10, whereas in normal tissue SUV $\approx$ 1. Two types of measurements will be made with this analysis. One will consist of drawing a ROI which will include the entire area of abnormal uptake from which an average SUV for the abnormality will be calculated. The other will consist of sampling the most active portion of the lesion to determine the maximum activity concentration in the tumor. While the former will be used to measure the overall tumor activity, the latter will be considered for grading the tumor. We are utilizing these quantitative measurements to monitor disease progression in individual subjects, after high-dose chemotherapy.

Results:

Thirty-one patients have until now been accrued in this protocol. Patient accrual is proceeding on schedule and as planned.

Since these patients are currently under protocol, we are accumulating data concerning clinical evaluation, biochemical tests, and correlative imaging methods. These will be analyzed when all PET studies will have been completed. An interim analysis of the results of the accuracy of the initial PET studies performed in a subset of 24 patients has been performed, and has been submitted for publication in the journal *Cancer*. The results of this analysis are reported below.

We have also implemented an iterative reconstruction algorithm (ordered subsets expectation maximization algorithm) to improve the image quality of whole-body studies and reduce artifacts produced by non uniform distribution of activity, especially in the thorax and the pelvis[20]. In our analysis of this algorithm, we have clearly shown significant improvements in image quality, with reduction of the noise content of the reconstructed images. Combined with improvements in our techniques of attenuation correction[21], we are able to achieve optimal quantitative whole-body studies for this protocol. These improvements are applied on all studies acquired for this protocol.

Qualitative interpretation:

Until now, 31 patients have had their initial PET studies before entering their high dose chemotherapy protocol. We have so far analyzed the results of the initial PET examinations in 24 of these patients to assess the prevalence of disease in metastatic breast cancer patients before high dose chemotherapy with stem cell rescue. The results of the PET studies were compared with the results of clinical examination and other radiological data, and are reported in tables 2 - 6.

Seventeen subjects had active disease demonstrated on the PET study (17/24, 81%), and in seven, no evidence of metabolically active disease was noted. In two subjects (8.3%), metastatic disease involvement was shown only on PET imaging (subjects 5, and 20 on table 2). In two subjects (subjects 8 and 24 on tables 2 and 4) with negative PET scans, residual lesions were shown only by bone scanning (8.3%). One of these subjects (subject 8) had a residual rib lesion that had responded well to conventional chemotherapy, and had become sclerotic on x-ray. The overall agreement with the combined restaging procedures was 83% (20/24, 95% confidence interval 68-98%, Kappa statistic 0.60), with FDG-PET demonstrating the presence of unsuspected disease in 2/7 (29%) patients thought to be free of measurable disease at the time of entry in the high dose chemotherapy trial.

Further analysis of the regional sensitivity of FDG-PET imaging indicates that this test is sensitive for detecting lymph node disease in the chest (table 3). In this area, FDG-PET imaging agreed with the conventional assessment in 20/24 subjects (83%, 95% confidence interval 68-94%). FDG-PET demonstrated the presence of hypermetabolic lymph node involvement in the chest in 8/24 patients. Only one of these patients had a positive CT in a corresponding site (subject 19, table 3), five had negative CT, while one patient had not undergone a restaging chest CT. Six of the eight patients with FDG-PET abnormalities in the mediastinum had evidence of metastatic disease elsewhere.

For the assessment of marrow involvement, FDG-PET was in good agreement with the bone scan results for the overall assessment of the presence of metastases (21/24 subjects, 87.5%, 95% confidence interval 68-97%, Kappa = 0.75). In the evaluation of liver disease, there was moderate overall agreement between PET and CT (17/24, 71%, 95% confidence interval 49-87%, Kappa = 0.26), but with more discrepancies than in other anatomic sites (Table 5).

We have also attempted to assess the accuracy of FDG-PET utilizing short-term outcome (6 months) with clinical and imaging follow-up as a "gold standard". Using these data to calculate the performance of FDG-PET, we obtained a sensitivity of 85% (95% confidence interval 62-97%), a specificity of 100% (40-100%), a positive predictive value of 100% (80 - 100%), and a negative predictive value of 57.1% (18-90%). These results are summarized in table 6.

Conclusion:

Our project ongoing successfully, and patient accrual is proceeding as planned. The initial data analysis confirmed the usefulness of FDG-PET imaging in restaging breast cancer. FDG-PET imaging provides unique independent information about disease activity in patients with breast cancer prior to high dose chemotherapy. The role of FDG PET in establishing prognosis and in assessing the outcome of treatment is being actively studied. Further subject accrual is underway and no difficulties are expected to achieve the goal of 40 subjects before the end of the year. We

believe the results of this study will be of considerable importance in the management of patients with breast cancer who are being considered for bone marrow transplantation.

References:

1. Reivich M, Alavi A. Positron emission tomography. New York: Alan R. Liss, Inc., 1985:478.
2. Brown RS, Wahl RL. Overexpression of Glut-1 glucose transporter in human breast cancer. An immunohistochemical study. Cancer 1993; 72:2979-85.
3. Clavo AC, Brown RS, Wahl RL. Fluorodeoxyglucose uptake in human cancer cell lines is increased by hypoxia. Journal of Nuclear Medicine 1995; 36:1625-32.
4. Brown RS, Leung JY, Fisher SJ, Frey KA, Ethier SP, Wahl RL. Intratumoral distribution of tritiated fluorodeoxyglucose in breast carcinoma: I. Are inflammatory cells important? Journal of Nuclear Medicine 1995; 36:1854-61.
5. Adler LP, Crowe JP, al-Kaisi NK, Sunshine JL. Evaluation of breast masses and axillary lymph nodes with [F-18] 2-deoxy-2-fluoro-D-glucose PET. Radiology 1993; 187:743-50.
6. Minn H, Soini I. [18F]fluorodeoxyglucose scintigraphy in diagnosis and follow up of treatment in advanced breast cancer. Eur J Nucl Med 1989; 15:61-6.
7. Nieweg OE, Wong WH, Singletary SE, Hortobagyi GN, Kim EE. Positron emission tomography of glucose metabolism in breast cancer. Potential for tumor detection, staging, and evaluation of chemotherapy. Ann N Y Acad Sci 1993; 698:423-8.
8. Nieweg OE, Kim EE, Wong WH, et al. Positron emission tomography with fluorine-18-deoxyglucose in the detection and staging of breast cancer. Cancer 1993; 71:3920-5.
9. Wahl RL, Cody RL, Hutchins GD, Mudgett EE. Primary and metastatic breast carcinoma: initial clinical evaluation with PET with the radiolabeled glucose analogue 2-[F-18]-fluoro-2-deoxy-D-glucose. Radiology 1991; 179:765-70.

10. Crowe JP, Jr., Adler LP, Shenk RR, Sunshine J. Positron emission tomography and breast masses: comparison with clinical, mammographic, and pathological findings. Ann Surg Oncol 1994; 1:132-40.

11. Adler L, Cascade E, Crowe J, et al. Clinical application and economic implications of PET in the assessment of axillary lymph node involvement in breast cancer: a retrospective study. Abstract from the 1994 ICP meeting. Fairfax: Institute for Clinical PET, 1994.

12. Wahl RL, Zasadny K, Helvie M, Hutchins GD, Weber B, Cody R. Metabolic monitoring of breast cancer chemohormonotherapy using positron emission tomography: initial evaluation. J Clin Oncol 1993; 11:2101-11.

13. Huovinen R, Leskinen-Kallio S, Nagren K, Lehikoinen P, Ruotsalainen U, Teras M. Carbon-11-methionine and PET in evaluation of treatment response of breast cancer. Br J Cancer 1993; 67:787-91.

14. Jansson T, Westlin JE, Ahlstrom H, Lilja A, Langstrom B, Bergh J. Positron emission tomography studies in patients with locally advanced and/or metastatic breast cancer: a method for early therapy evaluation? J Clin Oncol 1995; 13:1470-7.

15. Karp JS, Muehllehner G. Standards for performance measurements of PET scanners: evaluation with the UGM PENN-PET 240H scanner. Med Prog Technol 1991; 17:173-87.

16. Karp JS, Daube-Witherspoon ME, Muehllehner G. Factors affecting accuracy and precision in PET volume imaging. J Cereb Blood Flow Metab 1991; 11:A38-44.

17. Hudson H, Larkin R. Accelerated image reconstruction using ordered subsets of projection data. IEEE Trans Med Imag 1994; MI-1:113-122.

18. Meikle S, Hutton B, Bailey D, Hooper P, Fulham M. Accelerated EM reconstruction in total-body PET: potential for improving tumor detectability. Phys Med Biol 1994; 39:1689-1709.

19. Zasadny KR, Wahl RL. Standardized uptake values of normal tissues at PET with 2-[fluorine-18]-fluoro-2-deoxy-D-glucose: variations with body weight and a method for correction. Radiology 1993; 189:847-50.

20. Benard F, Smith R, Karp J, Ozdemir S, Alavi A. Improved image quality of whole-body FDG-PET scans by employing a practical algorithm: expectation maximization with ordered subsets (EM-OS). J Nucl Med 1996; 37:130P.

21. Smith R, Benard F, Alavi A, Karp J. An optimized protocol for attenuation corrected, whole-body FDG-PET images of cancer patients (Abstract). Eur J Nucl Med 1996; 23:1123.

TABLE 1: PET qualitative rating scheme

PET Rating scale:
0: Normal scan
1: Probably normal scan
2: Possibly abnormal scan
3: Probably abnormal scan
4: Definitely abnormal scan

Grades 0-1 were considered negative, and 2-4 positive.

TABLE 2: FDG-PET imaging in the assessment of residual disease compared to combined clinical evaluation and conventional imaging procedures

No	*PET result*	*PET Grade*	*Other Imaging*	*Global clinical*
1	+	4	+	R
2	+	4	+	R
3	-	1	-	ND
4	-	0	-	ND
5	+	4	-	ND
6	+	4	+	R
7	+	4	+	R
8	-	1	+	R
9	+	3	-	ND
10	+	4	+	R
11	+	3	+	R
12	+	4	+	R
13	-	1	-	ND
14	-	1	-	ND
15	+	4	+	R
16	+	4	+	R
17	-	0	-	ND
18	+	3	+	R
19	+	3	+	R
20	+	4	-	ND
21	+	3	+	R
22	+	4	+	R
23	+	4	+	R
24	-	0	+	R

"=": Equivocal result
"+": Positive result
"-": Negative result
"R": Partial response to previous chemotherapy
"ND": No demonstrable disease

2x2 Table

FDG-PET	Clinical/Imaging +	Clinical/Imaging -	Total
+	*15*	*2*	17
-	*2*	*5*	7
Total	17	7	24

TABLE 3 – Assessment of thoracic disease

	FDG-PET				*CT/Chest x-ray*			
No	*Lungs*	*Grade*	*Nodes*	*Grade*	*Chest CT?*	*Lungs*	*Nodes*	*Extent*
1	-	0	+	4	y	-	-	PET>CT
2	-	1	-	0	n	-	-	=
3	-	0	-	0	y	-	-	=
4	-	0	-	0	y	-	-	=
5	-	0	+	4	y	-	-	PET>CT
6	-	0	+	4	y	+	-	PET>CT
7	-	0	+	4	y	-	-	PET>CT
8	-	1	-	0	y	-	-	=
9	-	0	+	3	y	+*	-	PET>CT
10	-	0	-	0	y	-	-	=
11	-	0	-	0	y	-	-	=
12	-	0	+	4	y	+**	-	PET>CT
13	-	1	-	0	y	-	-	=
14	-	0	-	1	n	-	-	=
15	-	0	-	0	y	-	-	=
16	-	0	-	0	y	-	-	=
17	-	0	-	0	n	-	-	=
18	+	2	+	3	n	-	-	PET>CxR
19	-	0	+	3	y	-	+	=
20	-	0	-	0	n	-	-	=
21	-	0	-	0	y	-	-	=
22	-	0	-	0	y	-	-	=
23	-	0	-	0	y	-	-	=
24	-	0	-	0	n	-	-	=

* residual 3 mm nodule in upper left lung; the patient had a history of pulmonary metastases that had almost completely disappeared after conventional chemotherapy.

** the CT study was obtained 73 days before the PET study, demonstrating axillary lesions which were surgically excised prior to FDG-PET. The PET scan was positive in the supraclavicular area, which was normal on that CT.

2x2 Table (presence of thoracic disease)

	Clinical/Imaging		**Total**
FDG-PET	**+**	**-**	
+	***4***	***4***	**8**
-	***0***	***16***	**16**
Total	**4**	**20**	**24**

TABLE 4 – Assessment of bone or marrow disease

No	*PET result*	*PET Grade*	*Bone scan*	*Extent*
1	-	0	-	=
2	+	4	+	BS>PET
3	-	0	-	=
4	-	0	-	=
5	-	0	-	=
6	+	4	+	BS>PET
7	-	0	+	BS>PET
8	-	0	+	BS>PET
9	-	0	-	=
10	+	4	+	=
11	+	3	+	=
12	-	0	-	=
13	-	0	=	=
14	-	0	-	=
15	+	4	+	BS>PET
16	+	4	+	PET>BS
17	-	0	-	=
18	+	3	+	BS>PET
19	-	0	-	=
20	-	0	-	=
21	+	3	+	=
22	+	4	+	PET>BS
23	+	4	+	PET>BS
24	-	0	+	BS>PET

2x2 Table

	Clinical/Imaging		**Total**
FDG-PET	**+**	**-**	
+	***10***	***0***	**10**
-	***3***	***11***	**14**
Total	**13**	**11**	**24**

TABLE 5 – Assessment of liver disease

No	*PET result*	*PET Grade*	*CT/MR result*	*Extent*
1	-	0	+	CT>PET
2	-	0	+	MR>PET
3	-	0	-	=
4	-	0	-	=
5	-	0	-	=
6	-	0	+	CT>PET
7	-	0	-	=
8	-	0	-	=
9	-	0	-	=
10	-	0	-	=
11	+	2	-	PET>CT
12	+	3	-	PET>CT
13	-	0	-	=
14	-	0	-	=
15	-	0	-	=
16	+	3	+	=
17	-	0	-	=
18	-	0	-	=
19	+	2	+	=
20	+	4	-	PET>CT
21	+	2	+	=
22	+	4	-	PET>CT
23	-	0	-	=
24	-	0	-	=

2x2 Table

	Clinical/Imaging		**Total**
FDG-PET	**+**	**-**	
+	***3***	***4***	**7**
-	***3***	***14***	**17**
Total	**6**	**18**	**24**

Table 6 - combined imaging data with short term follow-up

FDG-PET	Clinical/Imaging/ Follow-up +	-	Total
+	*17*	*0*	17
-	*3*	*4*	7
Total	20	4	24

Sensitivity =	85% (62 - 97%)
Specificity =	100% (40 - 100%)
Accuracy =	87.5% (68 - 97%)
Positive Predictive Value =	100% (80 - 100%)
Negative Predictive Value =	57% (18 - 90%)

The value reported is the percentage followed by the exact 95% confidence interval